UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,980	02/21/2002	John N. Feder	D0121.NP	9974

23914 7590 11/18/2002

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
10/080,980	FEDER ET AL.
Examiner	**Art Unit**
Daniel M Sullivan	1636

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

This is a First Office Action on the Merits of the Application filed February 21, 2001. This Office Action is a response to the Response to Restriction Requirement filed August 30, 2002 (Paper No. 6). The Preliminary Amendment filed August 30, 2002 (Paper No. 7) has been entered. Claims 1-19 were cancelled and claims 20-41 were added in Paper No. 7. Claims 20-41 are pending and under consideration in the application.

Election/Restrictions

Applicant's election of Group I, directed to an isolated nucleic acid molecule comprising SEQ ID NO:1 in its variant forms, vector, host cell, a method of making, and a method of diagnosing a pathological condition by determining the presence or absence of a mutation in the polynucleotide, in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20 and 30-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims of the instant application are directed to an isolated nucleic acid molecule comprising a polynucleotide sequence encoding the polypeptide set forth in the application as SEQ ID NO:2 or fragments thereof, polynucleotides comprising sequence complementary to said isolated nucleic acid molecule encoding the polypeptide set forth as SEQ ID NO:2 or fragments thereof, and polynucleotides capable of hybridizing under stringent conditions to the isolated nucleic acid molecule or encoding the polypeptide set forth as SEQ ID NO:2 or complementary sequences thereof. Claim 38 further comprises any nucleic acid molecule having at least 70% identity to any of the nucleic acid molecules to which claim 20 is directed. The claims are also directed to a vector and host cell comprising, and methods of using the nucleic acid molecules. The claims therefore encompass the broad genus of any and all nucleic acid molecules that comprise sufficient sequence identity with a any and all nucleic acid molecules encoding 50 or more contiguous amino acids of the polypeptide set forth as SEQ ID NO:2 to hybridize with said nucleic acid molecules encoding 50 or more contiguous amino acids of the polypeptide set forth as SEQ ID NO:2 under the stringency conditions set forth in page 15, lines 15-22 of the

specification, or having 70% identity thereto. It should be particularly pointed out that, to the extent the claims are directed to nucleic acid molecules capable of hybridizing to nucleic acid molecules encoding all or a portion of the polypeptide set forth as SEQ ID NO:2 or having 70% identity with nucleic acid molecules encoding all or a portion of the polypeptide set forth as SEQ ID NO:2, the claims encompass nucleic acid molecules that do not encode the polypeptide set forth as SEQ ID NO:2.

The Revised Interim Guidelines state "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus". "In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436). The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). In the instant case, Applicant has explicitly set forth a polypeptide sequence (i.e. SEQ ID NO:2) and a single nucleic acid species encoding the polypeptide sequence (i.e. SEQ ID NO:1). In addition, implicit in the description of a polypeptide is a description of all nucleic acid sequences capable of encoding that polypeptide. The disclosure does not, however, set forth an explicit or implicit description of a nucleic acid sequence that meets the limitation of "capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(f)" or "having a nucleotide sequence at least 70% identical to a sequence provided in claim 20" and that does not encode the polypeptide set forth as SEQ ID NO:2.

In the absence of a detailed description of a representative number of species, possession may be demonstrated by disclosure of the relevant identifying characteristics. The disclosure does not, however, provide a description of the relevant identifying characteristics of any and all nucleic acid molecules that are related to the explicit or implicitly described nucleic acid sequences encoding the polypeptide set forth as SEQ ID NO:2 by virtue of being able to hybridize to them or having 70% identity to them. According to the Revised Interim Guidelines, identifying characteristics include, "structure or other physical and or chemical properties....functional characteristics coupled with a known or disclosed correlation between function and structure or... a combination of such identifying characteristics..." (Federal Register, Vol. 66, No. 4, page 1106, column 3, second full paragraph). The ability of a DNA molecule to hybridize to another molecule or 70% identity is not a relevant identifying characteristic because the ability to hybridize or 70% identity at the nucleic acid level cannot be reliably correlated with the true function of the molecule (e.g. encode a protein or regulate expression of a gene).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of *any* and *all* nucleic acid molecules capable of hybridizing with a nucleic acid molecule comprising a polynucleotide sequence encoding the polypeptide sequence set forth as SEQ ID NO:2 or fragments thereof. Therefore, only the described polynucleotides comprising a nucleic acid sequence encoding a polypeptide set forth as SEQ ID NO:2 meet the written description provision of 35 U.S.C. §112, first paragraph.

With respect to the method claims and claims to a vector and host cell comprising the claimed nucleic acid molecule, adequate description first requires an adequate description of the materials, i.e. specific DNA sequences, which provide the means for making or using the invention.

Claims 20-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention: The instant application discloses a nucleic acid sequence encoding a protein, set forth as SEQ ID NO:2, which has limited similarity to the human potassium large conductance calcium-activated channel, subfamily M, and identity ranging from 23% to 60% to human, *D. melanogaster* and *C. elegans* proteins of unknown function. Applicant asserts, "[t]he polynucleotides or polypeptides...of the present invention can be used in assays to

test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that the molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides or polypeptides...could be used to treat the associated disease" (final paragraph on page 159 of the specification). Thus, Applicant has placed on the shoulders of the skilled artisan seeking to use the claimed polynucleotides the burden of: first, identifying the activity of the polynucleotides or encoded polypeptides; next, correlating that activity with a disease state; and finally, developing diagnostics or therapeutics from the claimed polypeptides. The issue at hand, therefore, is whether the skilled artisan would be able, provided the teachings of the specification and prior art, to develop diagnostics or therapeutics using the claimed polynucleotides without undue experimentation.

Breadth of the claims: The breadth of the claims is described herein above. To summarize, the claims are directed to any and all isolated nucleic acid molecules comprising a polynucleotide sequences encoding all or a portion of the sequence set forth as SEQ ID NO:2, any and all nucleic acid molecules capable of hybridizing with a nucleic acid molecule comprising a polynucleotide sequence encoding all or a portion of the sequence set forth as SEQ ID NO:2, and any and all nucleic acid molecules having at least 70% identity with a polynucleotide sequences encoding all or a portion of the sequence set forth as SEQ ID NO:2 capable of hybridizing therewith. Claims are also directed to vectors and host cells comprising the claimed polynucleotides and a method of diagnosing a pathological condition using the polynucleotide.

State of the prior art and level of predictability in the art: The prior art teaches MaxiK channel β-subunit genes from rat, mouse, bovine and canine (for example, see Jiang *et al.* (1999) *Genomics* 55:57-67 and citations therein). Jiang *et al.* also teach that all five mammalian MaxiK β subunits have 191 amino acid residues of which 71% are identical in all species (see especially Fig. 5 and the caption thereto, and the final paragraph on page 63). The prior art teaches K+Hnov27 and K+Hnov28 proteins, which are predicted to function as modulatory subunits for a K^+ channel although no empirical evidence is provided to support this supposition (see Miller *et al.* (1999; WO 99 43696). And, the prior art teaches a human hypothetical protein KIAA1317 (see attached NiceProt view of TrEMBL:Q9p2m9), *D. melanogaster* CG10830 (see attached NiceProt view of TrEMBL:Q9VDH3) and CG10465 proteins (see attached NiceProt view of TrEMBL:Q9V9F4), *C. elegans* protein VM106R.1 (see attached NiceProt view of TrEMBL:Q9XXA3), the functions of which are unknown as evidenced by the TrEMBL reports. None of these teachings provide a means to predict the function of a protein having limited identity to the proteins taught in the prior art. In the case of the only protein having an established function, the prior art teaches that all mammalian proteins having the function of a MaxiK channel β-subunit are highly conserved, having 71% identity over the full length of the protein across species. Therefore, the skilled artisan would not predict that a mammalian protein having no identity to the MaxiK channel β-subunit would have the same, or even a closely related function. In the case of predicting the function of a polypeptide based on similarity to proteins having unknown function, even if, for the sake of argument, the skilled artisan could predict with a high degree of certainty that the structurally related proteins had the same function, the function of the proteins remains unknown. Further, in the case of the proteins

having less than 50% identity, the skilled artisan would not predict related function unless it could be established that the proteins comprised regions of high identity that could be correlated with a known function.

Amount of direction provided by the inventor: Applicant teaches a polypeptide sequence having 0% identity and 37.5% similarity to the MaxiK channel β-subunit protein, and identities of 24% to CG10465, 30% to K+Hnov27 and K+Hnov28, 31% to *C. elegans* VM106R.1 protein, 51% with CG10830 and 60% with KIAA1317 (see especially Figure 4). Applicant also provides data from RNAi experiments with E4-1 cells that suggest that, "the physiological function of the CG10465 protein is to serve as a positive regulator in an innate immunity model in *Drosophila* cells..." (final paragraph on page 219 of the specification).

Existence of working examples: Neither the instant disclosure nor the prior art provide a function for the claimed polynucleotide or the encoded protein, any correlation between mutation of the claimed polynucleotide or encoded protein and a pathological condition, or a working example of a therapeutic or diagnostic comprising the claimed polynucleotide.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative skill in the art is very high, due to the high degree of uncertainty in predicting the function of the claimed polynucleotide or encoded polypeptide, the ordinary skilled artisan would not be able to achieve even the first step toward using the invention, without undue experimentation to establish the function of the polynucleotide or encoded polypeptide. The claimed polynucleotide and encoded polypeptide have very little identity with the only protein having a known function, i.e. the Maxi-K potassium channel β-subunit, or the only other protein for which functional data exists, i.e. CG10465. Further, in the

latter case functional data obtained using RNAi must be extrapolated not only from a polynucleotide encoding a protein having only 24% identity, but also from data obtained in insect cells to the mammalian organism. Therefore, given no more than the teachings available in the specification and prior art, the skilled artisan would have to resort to trial and error experimentation to establish the function of the claimed polypeptide before experiments to develop diagnostics or therapeutics could even be contemplated. This amount of experimentation would clearly be undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 25, 28-30 and 38 are rejected under 35 U.S.C. 102(a) as being anticipated by NCBI ENTREZ ACCESSION NO: gi:100473 available as of September 8, 2000 as evidenced by the notation in the first line of "COMMENT".

The claims are directed to an isolated nucleic acid molecule comprising a polynucleotide sequence selected from: encoding a polypeptide corresponding to amino acids 34 to 134 of SEQID NO:2; encoding 50contiguous amino acids of SEQ ID NO:2; a complementary sequence of those recited above or fragment thereof; capable of hybridizing under stringent conditions to

any of the above nucleic acid molecules; or having 70% identity to any of the above nucleic acid molecules.

NCBI ENTREZ ACCESSION NO: gi:100473 teaches all of the limitations of the claimed nucleic acid molecule (see attached sequence alignment bridging pages 5 and 6). NCBI ENTREZ ACCESSION NO: gi:100473 therefore anticipates the claims.

Claims 20-26, 28-30 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by NCBI ENTREZ ACCESSION NO: gi:1931504.

The claims are directed to an isolated nucleic acid molecule comprising a polynucleotide sequence selected from: encoding a polypeptide corresponding to amino acids 1 or 2 to 325; encoding a polypeptide corresponding to amino acids 34 to 134 of SEQID NO:2; encoding 50contiguous amino acids of SEQ ID NO:2; a complementary sequence of those recited above or fragment thereof; capable of hybridizing under stringent conditions to any of the above nucleic acid molecules; or having 70% identity to any of the above nucleic acid molecules.

NCBI ENTREZ ACCESSION NO: gi:1931504 teaches all of the limitations of the claimed nucleic acid molecule (see attached sequence alignment page 4). NCBI ENTREZ ACCESSION NO: gi:1931504 therefore anticipates the claims.

Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
November 8, 2002

JAMES KETTER
PRIMARY EXAMINER